UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,133	02/22/2002	Barry A. Morgan	00537-190002	8080

7590 02/14/2005

Brian R Morrill
Biomeasure Incorporated
27 Maple Street
Milford, MA 01757

EXAMINER	
WAX, ROBERT A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Supplemental Notice of Allowability	Application No.	Applicant(s)	
	09/980,133	MORGAN ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *discovery of defects in the claims*.

2. ☒ The allowed claim(s) is/are *2-26*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER

02112005

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

Please see the attached Examiner's Amendment which corrects some problems with the claims that were discovered.

Robert A. Wax
Primary Examiner
Art Unit: 1653

SUPPLEMENTAL EXAMINER'S AMENDMENT

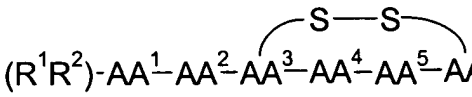
1. An examiner's amendment to the record appears below. This amendment is necessitated by the discovery of inconsistencies within the claims, for example, when claim 1 was canceled its definitions for some of the variables were not added to claim 2. This amendment corrects the discovered problems. A clean copy of the allowed claims is enclosed with this Office action and made a part of the official record.

2. Authorization for this examiner's amendment was given in a telephone interview with Alan F. Feeney on January 11, 2005.

3. The application has been amended as follows:

1 (canceled)

2 (currently amended): A compound ~~according to claim 1, wherein said compound is~~ of formula (II):



(II)

or a pharmaceutically acceptable salt thereof,
wherein
the α-nitrogen of AA^1, AA^2, AA^3, AA^4, AA^5, AA^6, AA^7, and AA^8 each is, independently, optionally substituted with (C_{1-4})alkyl, (C_{3-4})alkenyl, (C_{3-4})alkynyl, or (C_{1-6})alkyl-C(O)-;
AA^1 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Aac, Aic, Arg, Asn, Asp, Dip, Gln, Glu, Hyp, Lys, Mac, Macab, Orn, Pip, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Pip, hArg, Bip, Bpa, Tic, Cmp, [[,]] Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, [[,]] Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia,

Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α-Chpa, Cit, Nua, Pyp and an optionally substituted aromatic α-amino acid,

wherein said optionally substituted aromatic α-amino acid is optionally substituted with one or more substituents selected from the group consisting of halogen, NO_2, OH, CN, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, and NR^9R^{10};

AA^2 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Aic, Arg, Hca, His, Hyp, Pal, F_5-Phe, Phe, Pro, Trp, X^0-Phe, Pip, hArg, Bip, Bpa, Tic, Cmp, [[,]] Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, [[,]] Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α-Chpa, Cit, Nua, and ~~Pyp;AA^3~~ Pyp; AA^3 is the D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa and Tmpa;

AA^4 is a D- or L-isomer of an amino acid selected from the group consisting of Trp, N-Met-Trp, β-Met-Trp, His, hHis, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and an optionally substituted aromatic α-amino acid,

wherein said optionally substituted aromatic α-amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO_2, OH, (C_{1-4})alkyl, (C_{2-4})alkenyl, (C_{2-4})alkynyl, Bzl, O-Bzl, and NR^9R^{10};

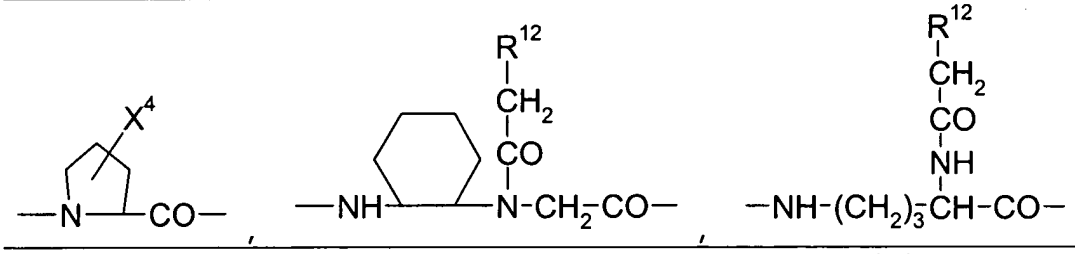
AA^5 is a D- or L-isomer of an amino acid selected from the group consisting of 4-Pip-Gly, 4-Pip-Ala, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, hLys, Lys, Orn, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala,

wherein the side-chain amino group of said amino acid is optionally mono- or di-substituted with R^3 and R^4;

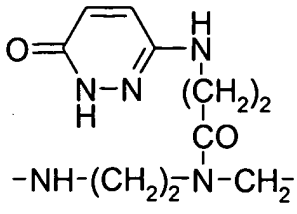
AA^6 is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, and Tmpa;

AA^7 is absent or a D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Aic, A3c, A4c, A5c, A6c, Abu, Aib, β-Ala, Arg, Bpa, Cha, Deg, Gaba, His, Ile, Leu, Nal, Nle, Pal, Phe, F_5-Phe, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, N-Me-

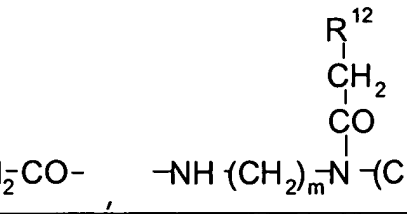
Trp, Val, N-Me-Val, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and X^0-Phe;
AA^8 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, an optionally substituted aromatic α-amino acid, Maa, Maaab, Ser, Ser(Bzl), Thr, Thr(Bzl), Tyr, Phe(4-O-Bzl), F_5-Phe, and X^5-Phe;
R^1 and R^2 each is, independently, H, E-, $E(O)_2S$-, E(O)C-, EOOC-, R^{13}, or absent;
R^3 and R^4 each is, independently, (C_{1-12})alkyl, (C_{2-12})alkenyl, (C_{2-12})alkynyl, phenyl, naphthyl, phenyl-(C_{1-6})alkyl, phenyl-(C_{2-6})alkenyl, phenyl-(C_{2-6})alkynyl, naphthyl-(C_{1-6})alkyl, naphthyl-(C_{2-6})alkenyl, naphthyl-(C_{2-6})alkynyl, (cyclo(C_{3-7})alkyl)-(C_{1-6})alkyl, (cyclo(C_{3-7})alkyl)-(C_{2-6})alkenyl, (cyclo(C_{3-7})alkyl)-(C_{2-6})alkynyl, heterocyclyl-(C_{1-4})alkyl, heterocyclyl-(C_{2-4})alkenyl, heterocyclyl-(C_{2-4})alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl, or benzhydryl;
R^5 is $-OR^6$, $-NR^7R^8$, or absent,
wherein each R^6, R^7 and R^8 is, independently, H, (C_{1-12})alkyl, (C_{2-12})alkenyl, (C_{2-12})alkynyl, phenyl, naphthyl, phenyl-(C_{1-6})alkyl, phenyl-(C_{2-6})alkenyl, phenyl-(C_{2-6})alkynyl, naphthyl-(C_{1-6})alkyl, naphthyl-(C_{2-6})alkenyl, naphthyl-(C_{2-6})alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl, or benzhydryl;
R^9 and R^{10} each is, independently, H, (C_{1-6})alkyl, (C_{3-4})alkenyl, (C_{3-4})alkynyl, 1-adamantyl, or 2-adamantyl;
R^{11} is, independently for each occurrence, a D- or L-amino acid of the formula:



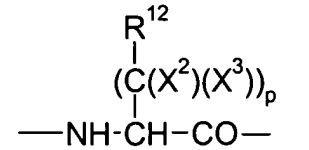
(1) (2) (3)



(4),



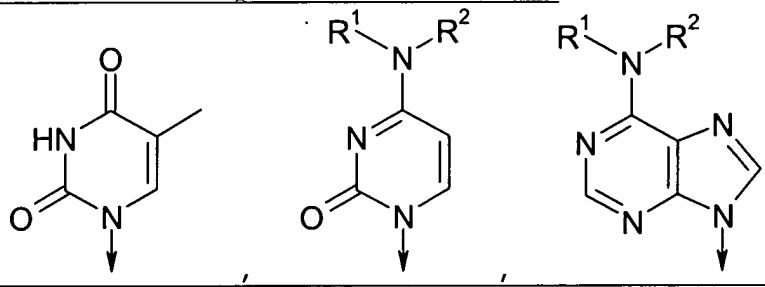
(5), or



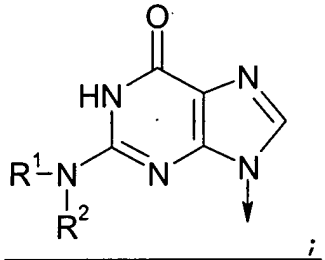
(6),

wherein m and n each is, independently, 1, 2, or 3, and p is 0, 1, or 2;

R^{12} is, independently for each occurrence, an optionally substituted moiety of the formula:

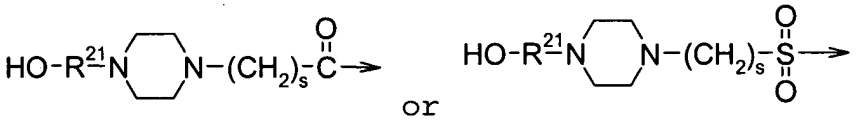


, , , or



;

R^{13} is a moiety according to the formula



or

,

wherein R^{21} is (C_{1-4})alkyl and s is 1, 2, 3, or 4;

E is, independently for each occurrence, an optionally substituted moiety selected from the group consisting of (C_{1-12})alkyl, (C_{2-12})alkenyl, (C_{2-12})alkynyl, phenyl, naphthyl, phenyl-

(C_{1-6})alkyl, phenyl-(C_{2-6})alkenyl, phenyl-(C_{2-6})alkynyl, naphthyl-(C_{1-6})alkyl, naphthyl-(C_{2-6})alkenyl, naphthyl-(C_{2-6})alkynyl, (cyclo(C_{3-7})alkyl)-(C_{1-6})alkyl, (cyclo(C_{3-7})alkyl)-(C_{2-6})alkenyl, (cyclo(C_{3-7})alkyl)-(C_{2-6})alkynyl, heterocyclyl-(C_{1-4})alkyl, heterocyclyl-(C_{2-4})alkenyl, heterocyclyl-(C_{2-4})alkynyl, 1-adamantyl, 2-adamantyl, dicyclopropylmethyl, dimethylcyclopropylmethyl, 9-fluorenylmethyl, and benzhydryl;

wherein the optionally substituted moiety defined for E is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, OH, Bzl, O-Bzl, NO_2, CN, COOH, and SH;

~~and~~

X^0 is halogen, NO_2, CH_3, OH, Bzl, O-Bzl or CN;

X^1 is H, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, indolyl, imidazolyl, 1-naphthyl, 3-pyridyl, optionally ring-substituted benzyl, or a moiety which corresponds to the side-chain group of Arg, Leu, Gln, Lys, Tyr, His, Thr, Trp, Phe, Val, Ala, Lys, or His;

wherein said optionally ring-substituted benzyl is optionally substituted with one or more substituents selected from the group consisting of halogen, OH, (C_{1-6})alkoxy, mono- or di-(C_{1-6})alkylamino, (C_{1-4}) alkyl, (C_{2-4}) alkenyl, (C_{2-4}) alkynyl, and NR^9R^{10};

X^2 and X^3 each is, independently, H, halogen, OH, =O, =S, (C_{1-12})alkyl, (C_{2-12})alkenyl, (C_{2-12})alkynyl, phenyl, naphthyl, phenyl-(C_{1-6})alkyl, phenyl-(C_{2-6})alkenyl, phenyl-(C_{2-6})alkynyl, naphthyl-(C_{1-6})alkyl, naphthyl-(C_{2-6})alkenyl, naphthyl-(C_{2-6})alkynyl, (cyclo(C_{3-7})alkyl)-(C_{1-6})alkyl, (cyclo(C_{3-7})alkyl)-(C_{2-6})alkenyl, (cyclo(C_{3-7})alkyl)-(C_{2-6})alkynyl, heterocyclyl-(C_{1-4})alkyl, heterocyclyl-(C_{2-4})alkenyl, heterocyclyl-(C_{2-4})alkynyl, 1-adamantyl, 2-adamantyl, dicyclopropylmethyl, or dimethylcyclopropyl methyl;

X^4 is H, OH, or NH_2; and

X^5 is halogen, NO_2, CH_3, OH, Bzl or O-Bzl;

provided that:

at least one of AA^7 or AA^8 is present[[.]];

at least six amino acid residues are present;

when AA^1 is a D- or L-isomer of an amino acid selected from the group consisting of Mac or Macab, then AA^8 is a D- or L-

isomer of an amino acid selected from the group consisting of Maa and Maaab, and when AA^8 is a D- or L-isomer of an amino acid selected from the group consisting of Maa and Maaab, then AA^1 is a D- or L-isomer of Mac or of Macab, and AA^1 is connected by a disulfide bond with AA^8;

AA^2 can be D- or L-Hca only when AA^1 is absent;

when one of R^1 or R^2 is $E(O)_2S$-, E(O)C-, EOOC-, or R^{13}, the other is H;

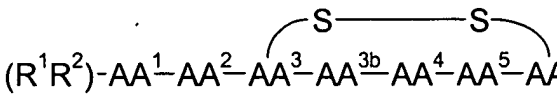
when R^5 is absent, then one of R^1 or R^2 is also absent, and the N-terminal amino acid and C-terminal amino acid together form an amide bond;

when one of X^2 or X^3 is C=O or C=S, the other is absent; and

said compound of formula (I) is not of the formula:

D-4-NO_2-Phe-Phe(4-O-Bzl)-cyclo(D-Cys-D-Trp-Lys-Cys)Cha-Nal-NH_2; or
D-4-NO_2-Phe-cyclo(D-Cys-Phe(4-O-Bzl)-D-Trp-Lys-Cys)-Val-Tyr-NH_2.

3 (currently amended): A compound ~~according to claim 1, wherein said compound is~~ of formula (III):



(III)

or a pharmaceutically acceptable salt thereof,
wherein
AA^1 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Aac, Aic, Arg, Asn, Asp, Gln, Glu, Hca, His, Hyp, Lys, Mac, Macab, Orn, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Pip, hArg, Bip, Bpa, Tic, Cmp, [[,]] Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, [[,]] Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α-Chpa, Cit, Nua, Pyp and an optionally substituted aromatic α-amino acid,

wherein said optionally substituted aromatic α-amino acid is optionally substituted with one or more substituents selected from the group consisting of halogen, NO_2, OH, CN, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, and NR^9R^{10};

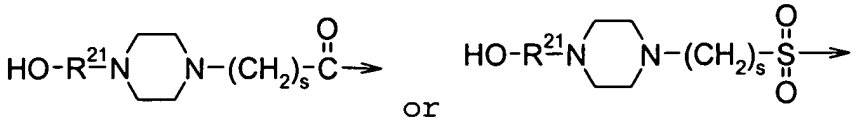
AA^3 is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, and Tmpa;
AA^{3b} is the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Arg, Bpa, F_5-Phe, His, Nal, Pal, 4-Pal, Phe, Trp, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and X^5-Phe;
AA^4 is a D- or L-isomer of an amino acid selected from the group consisting of Trp, N-Met-Trp, β-Met-Trp, His, hHis, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and an optionally substituted aromatic α-amino acid;

wherein said optionally substituted aromatic α-amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO_2, OH, CN, (C_{1-4})alkyl, (C_{2-4})alkenyl, (C_{2-4})alkynyl, Bzl, O-Bzl, and NR^9R^{10};

AA^5 is a D- or L-isomer of an amino acid selected from the group consisting of 4-Pip-Gly, 4-Pip-Ala, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, hLys, Lys, ~~and~~ Orn, ~~and,~~ hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala,

wherein the side-chain amino group of said amino acid is optionally mono- or di-substituted with R^3 and R^4;

AA^6 is a D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen, Tpa, and Tmpa;
AA^7 is absent or a D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Aic, A3c, A4c, A5c, A6c, Abu, Aib, β-Ala, Arg, Bpa, Cha, Deg, Gaba, His, Ile, Leu, Nal, Nle, Pal, Phe, F_5-Phe, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, N-Me-Trp, Val, N-Me-Val, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, and X^0-Phe;
X^0 is halogen, NO_2, CH_3, OH, CN, Bzl or O-Bzl;
R^1 and R^2 each is, independently, H, E-, $E(O)_2S$-, E(O)C-, EOOC-, R^{13}, or absent;
R^5 is $-OR^6$ or $-NR^7R^8$;
R^{13} is a moiety of the formula



wherein R^{21} is (C_{1-4})alkyl and s is 1, 2, 3, or 4;

provided that:

at least one of AA^1 or AA^2 is present;

when AA^1 is a D- or L-isomer of Pro, Hyp, Arg, Pip, hArg, Bip, Bpa, Tic, Cmp, [[,]] Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, [[,]] Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α-Chpa, Cit, Nua, Pyp or His, AA^2 cannot be a D- or L-isomer of Pro, Hyp, Arg, Pip, hArg, Bip, Bpa, Tic, Cmp, [[,]] Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, [[,]] Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, I-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, α-Chpa, Cit, Nua, Pyp or His;

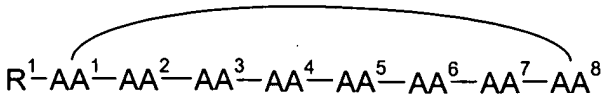
when AA^7 is a D- or L-isomer of Thr or of Ser, AA^8 cannot be a D- or L-isomer of Thr or of Ser;

at least one of AA^1, AA^2, AA^{3b}, AA^7, AA^{7b}, or AA^8 is the D- or L-isomer of R^{11}; and

when one of X^2 or X^3 is =O or =S, the other is absent;

or a pharmaceutically acceptable salt thereof.

4 (currently amended): A compound ~~according to claim 1, wherein said compound is~~ of formula (IV):



(IV)

wherein

AA^1 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Aic, Hyp, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Tic, Htic, Fala and an optionally substituted aromatic α-amino acid;

wherein said optionally substituted aromatic α-amino acid is optionally substituted with one or more substituents each independently selected from the group consisting of halogen, NO_2, OH, CN, (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{2-6})alkynyl, (C_{1-6})alkoxy, Bzl, O-Bzl, and NR^9R^{10};

AA^2 is absent or the D- or L-isomer of an amino acid selected from the group consisting of R^{11}, Arg, F_5-Phe, His, Pal, Phe, Trp, hArg, Pala, Bal, Fala, [[,]] Sala and X^0-Phe;

AA^3 is the D- or L-isomer of an optionally substituted aromatic α-amino acid,

wherein said optionally substituted aromatic α-amino acid is optionally substituted with one or more substituents selected from the group consisting of halogen, NO_2, OH, CN, (C_{1-4})alkyl, (C_{2-4})alkenyl, (C_{2-4})alkynyl, Bzl, O-Bzl, and NR^9R^{10};

AA^4 is a D- or L-isomer of an optionally substituted amino acid selected from the group consisting of Trp, N-Met-Trp, β-Me-Trp, Lys, Orn, hLys, *cis*-4-Acha, *trans*-4-Acha, *trans*-4-Amcha, 4-Pip-Gly, 4-Pip-Ala, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, and Pala;

wherein the side chain amino group of said optionally substituted amino acid is optionally substituted with R^3 and R^4;

AA^5 is absent or a D- or L-isomer of R^{11}, A3c, A4c, A5c, A6c, Abu, Aib, Aic, β-Ala, Bpa, Cha, Deg, F_5-Phe, Gaba, Ile, Leu, Nal, Nle, Pal, Phe, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, N-Me-Trp, Val, N-Me-Val, hArg, Bip, Tic, [[,]] Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala, or X^0-Phe;

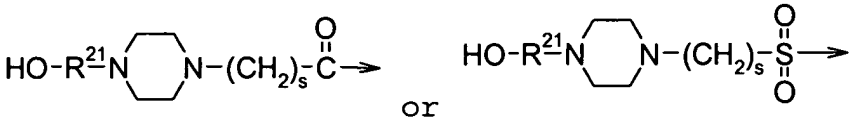
AA^6 is absent, the D- or L-isomer of R^{11}, an aromatic α-amino acid, F_5-Phe, Phe, Thr, Thr(Bzl), Ser, Ser(Bzl), or X^0-Phe;

AA^7 is absent, the D- or L-isomer of R^{11} or the D- or L-isomer of an aromatic α-amino acid;

AA^8 is a D- or L- isomer of R^{11};

R^1 is H, E-, $E(O)_2S$-, E(O)C-, EOOC-, or R^{13};

R^{13} is a moiety of the formula



or

wherein R^{21} is (C_{1-4})alkyl and s is 1, 2, 3, or 4;

X^0 in the definition of AA^2 and AA^5 is halogen, NO_2, OH, (C_{1-6})alkyl, (C_{1-6})alkoxy, mono- or di-(C_{1-6})alkylamino, Bzl or O-Bzl;
X^0 in the definition of AA^6 is halogen, NO_2, OH, (C_{1-6})alkyl, (C_{1-6})alkoxy, mono- or di-(C_{1-6})alkylamino, Bzl, O-Bzl, or NR^9R^{10};
provided that:

at least one of AA^1 or AA^2 is present;

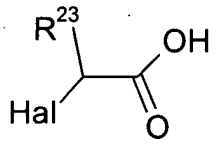
when AA^1 is absent, AA^2 and AA^8 together form a bond; and

at least two of AA^5, AA^6, and AA^7 are present;

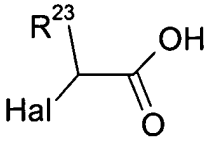
or a pharmaceutically acceptable salt thereof.

5 (original): A compound according to claim 2, wherein

AA^1 is absent, Ac-D-Phe, or the D- or L- isomer of R^{11}, Pip, Pro, or Ser, or of an aromatic α-amino acid selected from the group consisting of Cpa, Dip, Nal, Pal, and Phe;



AA^2 is absent, Aic, Pal, Phe, F_5-Phe, 4-NO_2-Phe, Trp, Tyr, Phe(4-O-Bzl)
AA^3 is the D- or L- isomer of an amino acid selected from the



group consisting of Pen, Cys, hCys and Tmpa;
AA^4 is the D- or L-isomer of Trp, His, N-Me-Trp, β-Me-Trp, hTrp, or hHis;
AA^5 is Lys, hLys, N-Me-Lys, Orn, cis-4-Acha or 4-Pip-Ala;
AA^6 is the D- or L-isomer of an amino acid selected from the group consisting of Cys, hCys, Pen and Tmpa;

AA^7 is A3c, A4c, A5c, A6c, Abu, Aic, β-Ala, Gaba, Nle, F_5-Phe, Phe, Pro, Sar, Ser, Thr, Thr(Bzl), Tyr, Val or absent; and
AA^8 is R^{11}, Nal, Thr, Thr(Bzl), Tyr, Phe(4-O-Bzl), or absent;
or a pharmaceutically acceptable salt thereof.

6 (original): A compound according to claim 5, wherein

AA^1 is absent or the D- or L- isomer of R^{11}, Pip or Pro, or of an aromatic α-amino acid selected from the group consisting of Cpa, Dip, Nal, Pal, Phe, and Ac-Phe;
AA^2 is Tyr, Pal, Phe, 4-NO_2-Phe, Trp, or absent;
AA^3 is a D- or L-isomer of Cys or Pen;
AA^4 is D-Trp;
AA^5 is Lys, Orn, or cis-4-Acha;
AA^6 is a D- or L-isomer of Cys or Pen;
AA^7 is A3c, A4c, A5c, A6c, Abu, Aic, β-Ala, Gaba, Nle, Phe, Pro, Sar, Thr, Thr(Bzl), Tyr, Val, or absent; and
AA^8 is R^{11}, Thr, Tyr, Nal, or absent;
or a pharmaceutically acceptable salt thereof.

7 (original): A compound according to claim 3, wherein

AA^1 is R^{11}, Aic, Hca, Pro, Ser, Ser(Bzl), Trp, Tyr, or a D- or L-isomer of an aromatic α-amino acid selected from the group consisting of Cpa, Nal, Ac-Nal, Phe, Ac-Phe, 4-NO_2-Phe, and Ac-4-NO_2-Phe;
AA^2 is Pal, Phe, F_5-Phe, Tyr, or absent;
AA^3 is a D- or L-isomer of Cys, hCys, Pen or Tmpa;
AA^{3b} is Pal, 4-Pal, His, Trp, Tyr, Phe(4-O-Bzl), Phe, or R^{11};
AA^4 is a D- or L-isomer of Trp or His;
AA^5 is Lys, N-Me-Lys, Orn, hLys, cis-4-Acha, or 4-Pip-Ala;
AA^6 is a D- or L-isomer of Cys, hCys, Pen or Tmpa;
AA^7 is R^{11}, A4c, A5c, Abu, β-Ala, Gaba, Phe, F_5-Phe, Ser(Bzl), Thr, Thr(Bzl), Phe(4-O-Bzl), or absent;
AA^{7b} is R^{11}, Nal, F_5-Phe, X^0-Phe or absent, wherein X^0 is halogen, NO_2, CH_3, OH, Bzl or O-Bzl; and
AA^8 is R^{11}, Nal, Tyr, Phe(4-O-Bzl), or absent;
or a pharmaceutically acceptable salt thereof.

8 (original): A compound according to claim 7, wherein

AA^1 is R^{11}, Aic, Hca, Pro, Ser(Bzl), or a D- or L-isomer of an aromatic α-amino acid selected from the group consisting of Cpa, Nal, Ac-Nal, Phe, Ac-Phe, 4-NO_2-Phe, and Ac-4-NO_2-Phe;
AA^2 is Pal, Tyr, or absent;
AA^3 is a D- or L-isomer of Cys or Pen;
AA^{3b} is R^{11}, Pal, 4-Pal, Trp, Tyr, Phe(4-O-Bzl), or Phe, wherein R^{11} is (T)aeg;
AA^4 is D-Trp;
AA^5 is Lys, N-Me-Lys, Orn, or cis-4-Acha;
AA^6 is a D- or L-isomer of Cys or Pen;
AA^7 is R^{11}, A5c, Abu, Ser(Bzl), Thr, Thr(Bzl), Phe(4-O-Bzl), Gaba, or absent;
AA^{7b} is Nal, X^0-Phe or absent; and
AA^8 is Tyr or absent;
or a pharmaceutically acceptable salt thereof.

9 (original): A compound according to claim 4, wherein

AA^1 is Aic, Hyp, Cpa, D-Cpa, Nal, Pal, Phe, Pro, R^{11}, Tyr or absent;
AA^2 is Phe, Trp, F_5-Phe, His, Tyr, Phe(4-O-Bzl), or R^{11};
AA^3 is a D-isomer of Trp, His, or Pal;
AA^4 is Lys, N-Me-Lys, Orn, hLys, cis-4-Acha, or 4-Pip-Ala;
AA^5 is Pal, Phe(4-O-Bzl), Thr(Bzl), Thr, Sar, Gaba, ß-Ala, A4c, A5c, A6c, Abu, Aic or absent;
AA^6 is Thr, Tyr, Ser, F_5-Phe, Cpa, Nal, or D- or L-Phe;
AA^7 is Nal, Pal, or absent; and
AA^8 is R^{11};
or a pharmaceutically acceptable salt thereof.

10 (original): A compound according to claim 9, wherein

AA^1 is Cpa, Nal, Pal, Phe, Tyr or absent;
AA^2 is Phe, Tyr, Trp, or R^{11};
AA^3 is D-Trp;
AA^4 is Lys, N-Me-Lys, or cis-4-Acha;
AA^5 is Pal, Phe(4-O-Bzl), Aic, Gaba, A5c or absent;
AA^6 is Thr, Nal, or D- or L-Phe;
AA^7 is absent; and

AA^8 is R^{11};
or a pharmaceutically acceptable salt thereof.

11 (original): A compound according to claim 2, wherein R^1 and R^5 are absent and the N-terminal amino acid and the C-terminal amino acid together form an amide bond; or a pharmaceutically acceptable salt thereof.

12 (original): A compound according to claim 3, wherein R^1 and R^5 are absent and the N-terminal amino acid and the C-terminal amino acid together form an amide bond; or a pharmaceutically acceptable salt thereof.

13 (original): A compound according to claim 6, wherein said compound is of the formula:

Ac-D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH_2;
Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
D-Dip-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
cyclo(D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr);
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A3c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A6c-Nal-NH_2;
(G(z))aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-ß-Ala-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Sar-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Pro-Nal-NH_2;
Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Nle-Phe-NH_2;
Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr-Nle-NH_2;
Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr-Phe-NH_2;
Cpa-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Gaba-NH_2;
Cpa-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Tyr-NH_2;

Pip-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-NH_2;
Pip-Phe-c(Cys-D-Trp-Lys-Cys)-Gaba-NH_2; or
Pro-Phe-c(D-Cys-D-Trp-Lys-D-Cys)-Thr-NH_2;
or a pharmaceutically acceptable salt thereof.

14 (original): A compound according to claim 6, wherein said compound is according to the formula:

Phe-cyclo(Cys-D-Trp-Lys-Cys)-Thr-NH_2;
Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH_2;
Ac-D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH_2;
Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A3c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A6c-Nal-NH_2;
(G(z))aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
D-Cpa-cyclo(Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-ß-Ala-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Sar-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Aic-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Pro-Nal-NH_2;
(T)aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-(A)aeg-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A4c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Nal-NH_2;
Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Nal-NH_2;
Pro-Phe-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-NH_2;
Pro-Phe-cyclo(D-Cys-D-Trp-Lys-Cys)-Val-NH_2;
Pip-4-NO2-Phe-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Nle-NH_2;
(G)aeg-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Thr(Bzl)-(C)aeg-NH_2;
or
(C)aeg-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Thr(Bzl)-(G)aeg-NH_2;
or a pharmaceutically acceptable salt thereof.

15 (original): A compound according to claim 8, wherein said compound is according to the formula

Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Phe-cyclo(Cys-Tyr-D-Trp-Lys-Cys)-Thr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Ac-D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-4-NO_2-Phe-Pal-cyclo(D-Cys-Phe(4-O-Bzl)-D-Trp-Lys-Cys)-Tyr-NH_2;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
D-Nal-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Pro-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Nal-NH_2;
Ser(Bzl)-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(G)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-4-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Phe-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Ser(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Phe(4-O-Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-A5c-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Abu-Tyr-NH_2;
D-Cpa-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(C)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
D-Cpa-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(Pen-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Trp-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Orn-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-hLys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Iamp-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Cha(4-am)-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Ser(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-D-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Trp-NH_2;

(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Pen)Thr(Bzl)-Tyr-NH_2;
(C)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
Ina-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
Mnf-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
Inp-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
Nua-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)Tyr(Bzl)-Thr-NH_2;
(C)aeg-Phe-c(D-Cys-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2; or
(T)aeg-D-Trp-c(D-Cys-Pal-Lys-D-Cys)Thr(Bzl)-Leu-NH_2;
or a pharmaceutically acceptable salt thereof.

16 (currently amended): A compound according to claim 8, wherein said compound is according to the formula

Hca-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Ac-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Ac-D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Ac-D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Phe-cyclo(Cys-Tyr-D-Trp-Lys-Cys)-Thr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Ac-D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-4-NO_2-Phe-Pal-cyclo(D-Cys-Phe(4-O-Bzl)-D-Trp-Lys-Cys)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
D-Nal-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Pro-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Nal-NH_2;
Ser(Bzl)-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(C)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Aic-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(C(z))aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(A(z))aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;

(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(G)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-4-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Phe-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Ser(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Phe(4-O-Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-A5c-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Abu-Tyr-NH_2;
D-Cpa-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-p-Me-Phe-NH_2;
Ac-(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Nal-NH_2;
D-Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Nal-NH_2;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
~~(C)aeg-~~
(C)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(C)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
D-Cpa-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(Pen-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Trp-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Orn-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-hLys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Iamp-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Cha(4-am)-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)-Ser(Bzl)-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-D-Tyr-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Cys)Thr(Bzl)-Trp-NH_2;
(T)aeg-c(D-Cys-Pal-D-Trp-Lys-D-Pen)Thr(Bzl)-Tyr-NH_2;
(C)aeg-c(D-Cys-Phe-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
Ina-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
Mnf-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
Inp-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
Nua-c(D-Cys-Phe-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2;
(T)aeg-Pal-c(D-Cys-D-Trp-Lys-D-Cys)Tyr(Bzl)-Thr-NH_2;
(C)aeg-Phe-c(D-Cys-D-Trp-Lys-D-Cys)Thr(Bzl)-Tyr-NH_2; or
(T)aeg-D-Trp-c(D-Cys-Pal-Lys-D-Cys)Thr(Bzl)-Leu-NH_2;
or a pharmaceutically acceptable salt thereof.

17 (original): A compound according to claim 10, wherein said compound is according to the formula

cyclo(Trp-D-Trp-Lys-Phe(4-O-Bzl)-Phe-(T)aeg);
cyclo(Trp-D-Trp-Lys-Pal-Phe -(T)aeg); or
cyclo(Phe-Phe-D-Trp-Lys-Thr-(T)aeg);
or a pharmaceutically acceptable salt thereof.

18 (original): A method of eliciting a neuromedin B receptor agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 13 or a pharmaceutically acceptable salt thereof.

19 (original): A method of eliciting a somatostatin receptor agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 14 or a pharmaceutically acceptable salt thereof.

20 (original): A method of eliciting a neuromedin B receptor agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 15 or a pharmaceutically acceptable salt thereof.

21 (original): A method of eliciting a somatostatin receptor agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 16 or a pharmaceutically acceptable salt thereof.

22 (original): A method of eliciting a somatostatin receptor agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 17 or a pharmaceutically acceptable salt thereof, provided said compound is not
cyclo(Trp-D-Trp-Lys-Phe(4-O-Bzl)-Phe-(T)aeg); or
cyclo(Trp-D-Trp-Lys-Pal-Phe -(T)aeg).

23 (original): A method of eliciting a SSTR-1 agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 14 or a pharmaceutically acceptable salt thereof, provided said compound is not

Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Nal-Tyr-cyclo(Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Abu-Nal-NH_2;
Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Nal-Tyr-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Val-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A3c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A6c-Nal-NH_2;
(G(z))aeg-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
D-Cpa-cyclo(Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-ß-Ala-Nal-NH_2;
cyclo(D-Cys-D-Trp-Lys-D-Cys)-A5c-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Sar-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Aic-Nal-NH_2;
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Gaba-Nal-NH_2; or
Cpa-Pal-cyclo(D-Cys-D-Trp-Lys-D-Cys)-Pro-Nal-NH_2.

24 (original): A method of eliciting a SSTR-1 agonist effect in a subject in need thereof, wherein said method comprises administering to said subject an effective amount of a compound according to claim 16 or a pharmaceutically acceptable salt thereof provided said compound is not

Ac-D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Ac-D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-Nal-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Nal-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
D-4-NO_2-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
4-NO_2-Phe-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;

D-Nal-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Pro-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Cpa-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Nal-NH_2;
Ser(Bzl)-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(C)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
Aic-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-D-Cys)-Thr(Bzl)-Tyr-NH_2;
(A)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(G)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-4-Pal-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Tyr-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Phe-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Ser(Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Phe(4-O-Bzl)-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-A5c-Tyr-NH_2;
(T)aeg-cyclo(D-Cys-Pal-D-Trp-Lys-Cys)-Abu-Tyr-NH_2; or
D-Cpa-cyclo(D-Cys-(T)aeg-D-Trp-Lys-Cys)-Thr(Bzl)-Tyr-NH_2.

25 (currently amended): A pharmaceutical composition comprising an effective amount of a compound according to claim ~~1~~ 2, 3 or 4 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier to treat a medical condition or disease in a subject wherein said medical condition or disease is from the list consisting of lung cancer, glioma, anorexia, hypothyroidism, hyperaldosteronism, H. pylori proliferation, acromegaly, restenosis, Crohn's disease, systemic sclerosis, external and internal pancreatic pseudocysts and ascites, VIPoma, nesidoblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison Syndrome, diarrhea, AIDS related diarrhea, chemotherapy related diarrhea, scleroderma, Irritable Bowel Syndrome, pancreatitis, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Cushing's Syndrome, gonadotropinoma, hyperparathyroidism, Graves' Disease, diabetic neuropathy, Paget's disease, polycystic ovary disease, thyroid cancer, hepatome, leukemia, meningioma, cancer cachexia,

orthostatic hypotension, postprandial hypotension, panic attacks, GH secreting adenomas, TSH secreting adenomas, prolactin secreting adenomas, insulinoma, glucagonoma, diabetes mellitus, hyperlipidemia, insulin insensitivity, Syndrome X, angiopathy, proliferative retinopathy, dawn phenomenon, Nephropathy, gastric acid secretion, peptic ulcers, enterocutaneous fistula, pancreaticocutaneous fistula, Dumping syndrome, watery diarrhea syndrome, pancreatitis, gastrointestinal hormone secreting tumor, angiogenesis, arthritis, allograft rejection, graft vessel bleeding, portal hypertension, gastrointestinal bleeding, obesity, and opioid overdose.

26 (currently amended): A method of treating a medical condition or disease in a subject, said method comprising administering to said subject a therapeutically effective amount of a compound of claim ~~1~~ 2, 3 or 4, wherein said medical condition or disease is selected from the list consisting of lung cancer, glioma, anorexia, hypothyroidism, hyperaldosteronism, H. pylori proliferation, acromegaly, restenosis, Crohn's disease, systemic sclerosis, external and internal pancreatic pseudocysts and ascites, VIPoma, nesidoblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison Syndrome, diarrhea, AIDS related diarrhea, chemotherapy related diarrhea, scleroderma, Irritable Bowel Syndrome, pancreatitis, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Cushing's Syndrome, gonadotropinoma, hyperparathyroidism, Graves' Disease, diabetic neuropathy, Paget's disease, polycystic ovary disease, thyroid cancer, hepatome, leukemia, meningioma, cancer cachexia, orthostatic

hypotension, postprandial hypotension, panic attacks, GH secreting adenomas, ~~Acromegaly~~, TSH secreting adenomas, prolactin secreting adenomas, insulinoma, glucagonoma, diabetes mellitus, hyperlipidemia, insulin insensitivity, Syndrome X, angiopathy, proliferative retinopathy, dawn phenomenon, Nephropathy, gastric acid secretion, peptic ulcers, enterocutaneous fistula, pancreaticocutaneous fistula, Dumping syndrome, watery diarrhea syndrome, pancreatitis, gastrointestinal hormone secreting tumor, angiogenesis, arthritis, allograft rejection, graft vessel bleeding, portal hypertension, gastrointestinal bleeding, obesity, and opioid overdose.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (571) 272-0623. The examiner can normally be reached on Monday through Friday, between 9:00 AM and 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Wax
Primary Examiner
Art Unit 1653

RAW